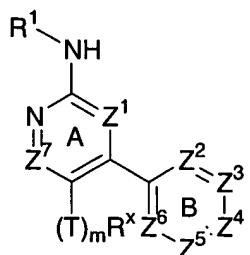


CLAIMS

1. A compound of formula I:



I

or a pharmaceutically acceptable salt thereof,

wherein:

R¹ is Q-Ar¹,

wherein Q is a C₁₋₂ alkylidene chain wherein one methylene unit of Q is optionally replaced by O, NR, NRCO, NRCONR, NRCO₂, CO, CO₂, CONR, OC(O)NR, SO₂, SO₂NR, NRSO₂, NRSO₂NR, C(O)C(O), or C(O)CH₂C(O);

Ar¹ is a 5-7 membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; wherein Ar¹ is optionally substituted with q independent occurrences of Z-R^Z; wherein q is 0-5, Z is a bond or is a C_{1-C₆} alkylidene chain wherein up to two non-adjacent methylene units of Z are optionally and independently replaced by CO, CO₂, COCO, CONR, OCONR, NRNR, NRNRCO, NRCO, NRCO₂, NRCONR, SO, SO₂, NRSO₂, SO₂NR, NRSO₂NR, O, S, or NR; and each occurrence of R^Z is independently selected from R', halogen, NO₂, CN, OR', SR', N(R')₂, NR'COR', NR'CON(R')₂, NR'CO₂R', COR', CO₂R', OCOR', CON(R')₂, OCON(R')₂, SOR', SO₂R', SO₂N(R')₂, NR'SO₂R', NR'SO₂N(R')₂, COCOR', or COCH₂COR';

each occurrence of R is independently hydrogen or an optionally substituted C₁₋₆ aliphatic group; and each occurrence of R' is independently hydrogen or an optionally substituted C₁₋₆

aliphatic group, a 3-8-membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; or R and R', two occurrences of R, or two occurrences of R', are taken together with the atom(s) to which they are bound to form an optionally substituted 3-12 membered saturated, partially unsaturated, or fully unsaturated monocyclic or bicyclic ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

Z¹ is N or CH;

Z⁷ is N or C(U)_nR^Y;

T and U are each independently a bond or a saturated or unsaturated C₁₋₆ alkylidene chain, wherein up to two methylene units of the chain are optionally and independently replaced by CO, CO₂, COCO, CONR, OCONR, NRNR, NRNRCO, NRCO, NRCO₂, NRCONR, SO, SO₂, NRSO₂, SO₂NR, NRSO₂NR, O, S, or NR;

m and n are each independently 0 or 1;

R^X and R^Y are each independently selected from R or Ar¹;

Z² is N or CR²; Z³ is N or CR³; Z⁴ is N or CR⁴; Z⁵ is N or CR⁵; and Z⁶ is N or CR⁶, wherein each occurrence of R², R³, R⁴, R⁵ or R⁶ is independently R^U or (V)_pR^V, provided that a) no more than three of Z², Z³, Z⁴, Z⁵ or Z⁶ is N, and b) at least one of Z³, Z⁴ or Z⁵ is CR³, CR⁴, or CR⁵, respectively, and at least one of R³, R⁴, or R⁵ is R^U,

each occurrence of R^U is NRCOR⁷, CONR(R⁷), SO₂NR(R⁷), NRSO₂R⁷, NRCONR(R⁷), NRSO₂NR(R⁷), or CONRNR(R⁷), wherein R⁷ is (CH₂)_t-Y-R⁸, and t is 0, 1, or 2, Y is a bond or is O, S, NR⁹, -OCH₂-, -SCH₂, -NR⁹CH₂, O(CH₂)₂-, -S(CH₂)₂, or -NR⁹(CH₂)₂, and R⁸ is Ar², or R⁸ and R⁹, taken together with the nitrogen atom, form an optionally substituted 5-8 membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen or sulfur;

each occurrence of V is a bond or a saturated or unsaturated C₁₋₆ alkylidene chain, wherein up to two methylene units of the chain are optionally and independently replaced by CO, CO₂, COCO, CONR, OCONR, NRNR, NRNRCO, NRCO, NRCO₂, NRCONR, SO, SO₂, NRSO₂, SO₂NR, NRSO₂NR, O, S, or NR;

each occurrence of p is 0 or 1;

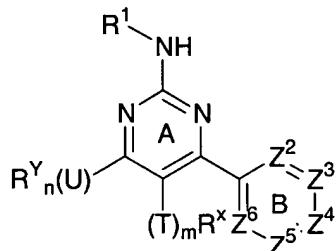
each occurrence of R^V is R or Ar^2 ; and

Ar^2 is a 5-7 membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; wherein Ar^2 is optionally substituted with r independent occurrences of $W-R^W$; wherein r is 0-3, W is a bond or is a C₁-C₆ alkylidene chain wherein up to two non-adjacent methylene units of W are optionally replaced by CO, CO₂, COCO, CONR, OCONR, NRNR, NRNRCO, NRCO, NRCO₂, NRCONR, SO, SO₂, NRSO₂, SO₂NR, NRSO₂NR, O, S, or NR; and each occurrence of R^W is independently selected from R', halogen, NO₂, CN, OR', SR', N(R')₂, NR'COR', NR'CON(R')₂, NR'CO₂R', COR', CO₂R', OCOR', CON(R')₂, OCON(R')₂, SOR', SO₂R', SO₂N(R')₂, NR'SO₂R', NR'SO₂N(R')₂, COCOR', or COCH₂COR';

provided that:

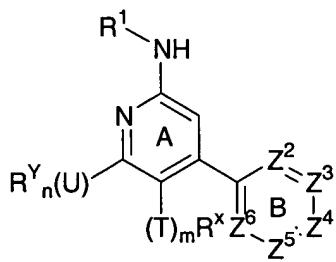
- a) when Z^1 is N, Z^7 is CH; and ring B is phenyl and at least one of R^3 or R^4 is NHCOR⁷, then R^1 is not phenyl only substituted with two or three occurrences of OR'; and
- b) when Z^1 is N, Z^7 is CH; and ring B is phenyl and at least one of R^3 or R^4 is NHCOR⁷, SO₂R⁷, CONRR⁷, then R^1 is not phenyl only substituted with one occurrence of -CON(R')₂ in the para position.

2. The compound according to claim 1, wherein Z^1 is N and the compound has the structure **II**:



II

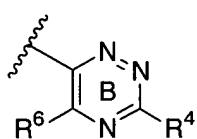
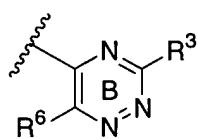
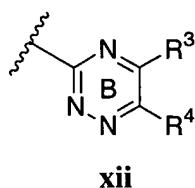
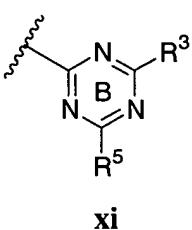
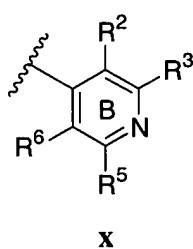
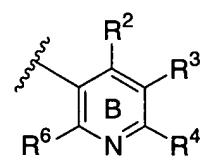
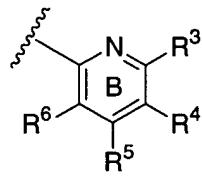
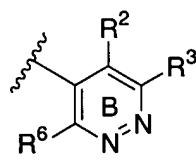
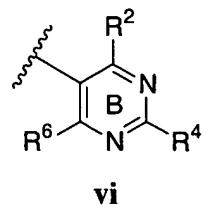
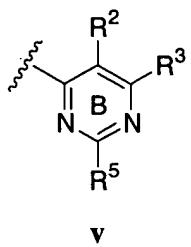
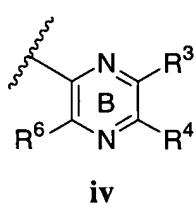
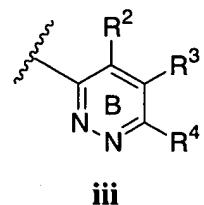
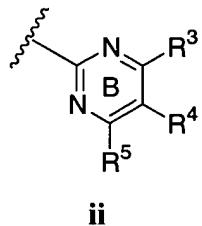
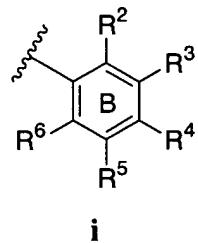
3. The compound of claim 1, wherein Z^1 is CH and amino pyridines of general formula **III** are provided:



4. The compound of claim 1, wherein R^1 is an optionally substituted phenyl, cyclohexyl, cyclopentyl, pyridyl, morpholino, piperazinyl, or piperidinyl group
5. The compound of claim 1, wherein R^1 is an optionally substituted from phenyl, cyclohexyl, or pyridyl group.
6. The compound of claim 1, wherein R^1 is optionally substituted phenyl.
7. The compound of claim 1, wherein q is 0, 1, 2, or 3 and each independent occurrence of ZR^Z is C_{1-4} alkyl, $N(R')_2$, OR' , SR' , $CON(R')_2$, $NR'COR'$, $NR'SO_2R'$, or $SO_2N(R')_2$.
8. The compound of claim 1, wherein q is 1 and ZR^Z is $-NH_2$, $-OH$, C_{1-4} alkoxy, or $-S(O)_2NH_2$.
9. The compound of claim 1, wherein q is 1, and ZR^Z is in the meta position and ZR^Z is $-NH_2$, $-OH$, C_{1-4} alkoxy, or $-S(O)_2NH_2$.
10. The compound of claim 1, wherein $(T)_mR^X$ and $(U)_nR^Y$ are hydrogen, halogen, NO_2 , CN , OR , SR or $N(R)_2$, or C_{1-4} aliphatic optionally substituted with oxo, OR , SR , $N(R)_2$, halogen, NO_2 or CN .
11. The compound of claim 1, wherein $(T)_mR^X$ and $(U)_nR^Y$ are each independently hydrogen, Me , OH , OMe or $N(R)_2$.

12. The compound of claim 1, wherein $(T)_m R^X$ and $(U)_n R^Y$ are each hydrogen.

13. The compound of claim 1, wherein ring B is one of rings i-xiv:



14. The compound of claim 1, wherein t is 0, Y is a bond, and R⁸ is an optionally substituted aryl or heteroaryl moiety.

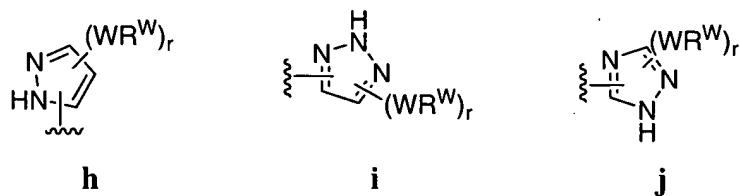
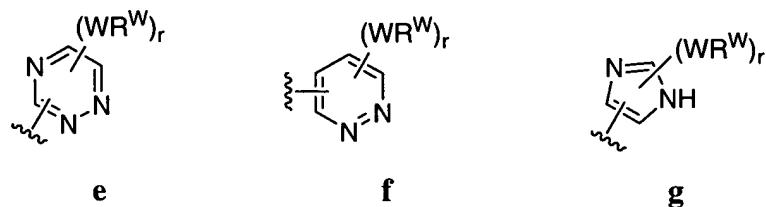
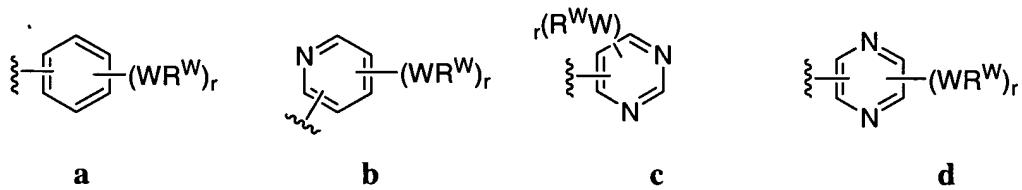
15. The compound of claim 1, wherein t is 0, Y is a bond, and R⁸ is an optionally substituted heteroaryl moiety.

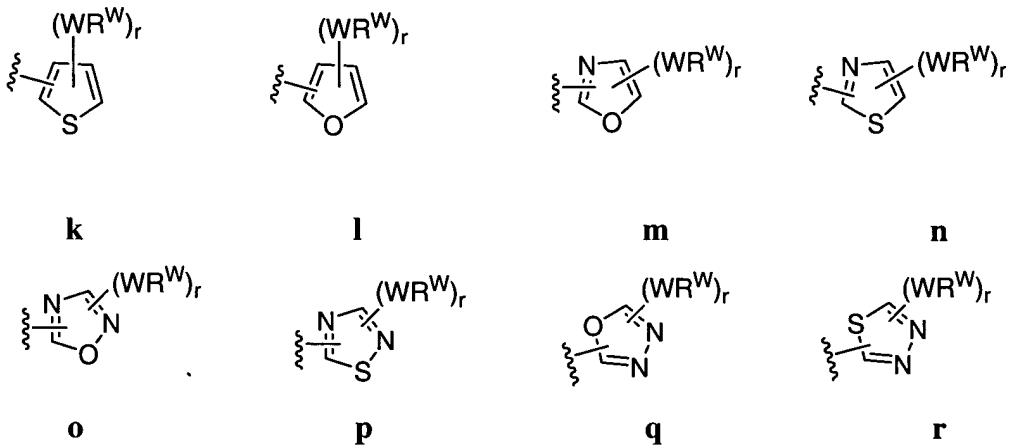
16. The compound of claim 1, wherein R⁷ is -CH₂-Y-R⁸, and Y is NR⁹, O or S, and R⁸ is an optionally substituted aryl or heteroaryl moiety.

17. The compound of claim 1, wherein R⁷ is -CH₂-Y-R⁸, and Y is NR⁹, O or S, and R⁸ is an optionally substituted aryl moiety.

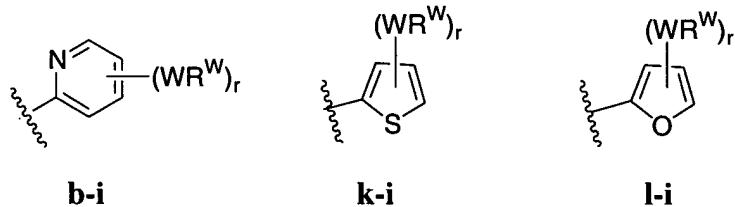
18. The compound of claim 1, wherein t is 0 or 1, Y is NR⁹, and R⁸ and R⁹, taken together with the nitrogen atom, form a 5-8 membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen or sulfur.

19. The compound of claim 1, wherein R⁸ is a 5- or 6-membered aryl or heteroaryl group having one of the formulae:

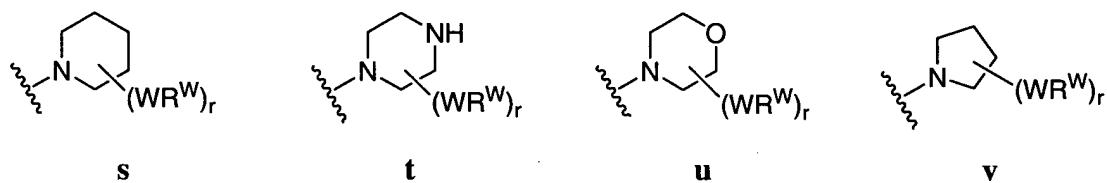




20. The compound of claim 1, wherein R⁸ is a 5- or 6-membered heteroaryl group having one of the formulae:



21. The compound of claim 1, wherein R⁸ and R⁹, taken together, form a group having one of the formulae:



22. The compound of claim 1, wherein r is 0 or 1.

23. The compound of claim 19, 20, or 21, wherein r is 1, 2, or 3, and each occurrence of halogen, C₁₋₄alkyl, -(R)₂, -OR, -SR, -SO₂N(R)₂, -N(R)SO₂R, -N(R)COR, -N(R)₂, -CH₂OR, -CH₂N(R)₂, or -CH₂SR.

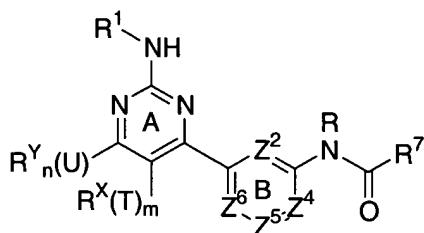
24. The compound of claim 19, 20, or 21, wherein t is 0, Y is a bond, and R⁸ is an optionally substituted heteroaryl moiety selected from one of groups **b** through **r**.

25. The compound of claim 24, wherein R⁸ is an optionally substituted heteroaryl group **b-i**, **k-i**, or **l-i**.

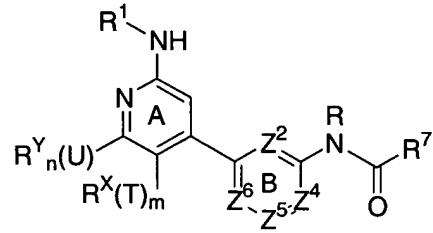
26. The compound of claim 1, wherein t is 1, Y is O, S or NR⁹, and R⁸ is optionally substituted phenyl.

27. The compound of claim 1, wherein t is 0 or 1, Y is NR⁹, and R⁸ and R⁹, taken together form an optionally substituted group selected from **s**, **u** or **v**.

28. The compound of claim 1, wherein Z³ or Z⁵ is CR³ or CR⁵, respectively, and R³ or R⁵ is NRC(O)R⁷, wherein R⁷ is (CH₂)_t-Y-R⁸, wherein t is 0, 1 or 2, wherein Y is a bond or is O, S, NR⁹, -OCH₂-, -SCH₂, -NR⁹CH₂, O(CH₂)₂-, -S(CH₂)₂, or -NR⁹(CH₂)₂, and wherein R⁸ is Ar², or R⁸ and R⁹, taken together with the nitrogen atom, form a 5-8 membered heterocyclil or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen or sulfur, and compounds have the formula **II-A** or **III-A**:

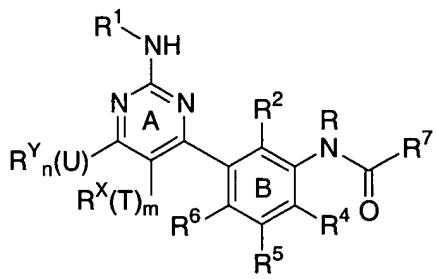


II-A

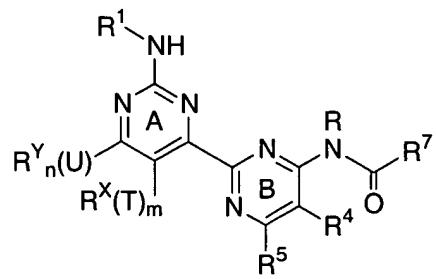


III-A

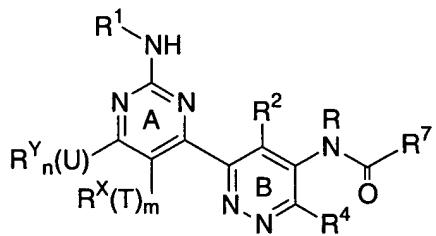
29. The compound of claim 28, wherein for compounds of formula **II-A** ring B is selected from **i**, **ii**, **iii**, **iv**, **v**, **vii**, **viii**, **ix**, **x**, **xi**, **xii**, or **xiii** and compounds have one of formulas **II-A-i**, **II-A-ii**, **II-A-iii**, **II-A-iv**, **II-A-v**, **II-A-vii**, **II-A-viii**, **II-A-ix**, **II-A-x**, **II-A-xi**, **II-A-xii**, or **II-A-xiii**:



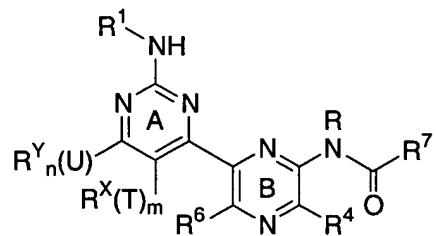
II-A-i



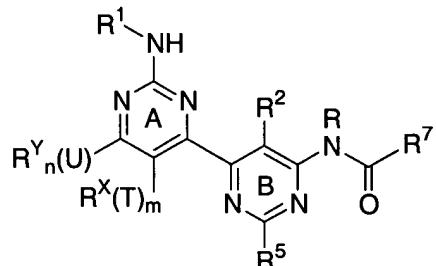
II-A-ii



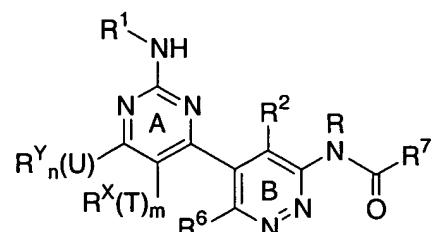
II-A-iii



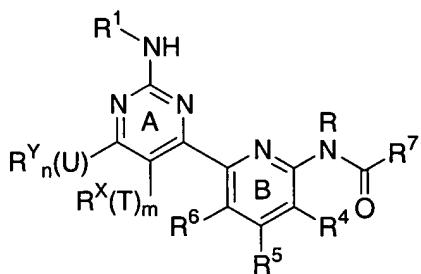
II-A-iv



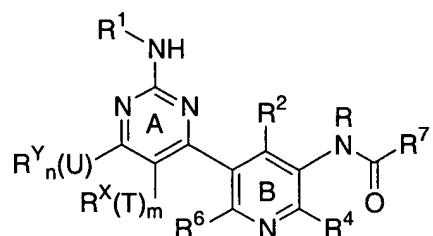
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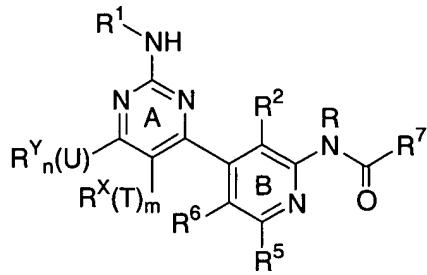
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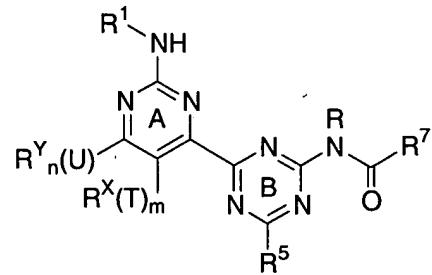
II-A-viii



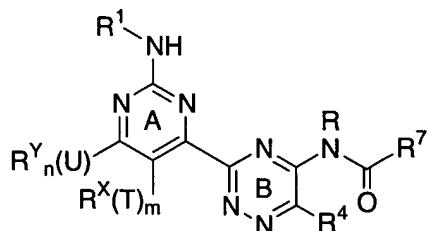
II-A-ix



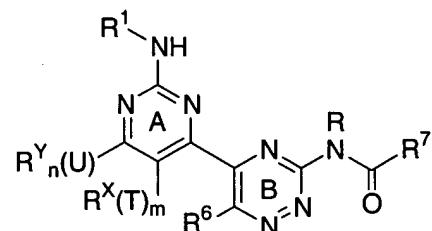
II-A-x



II-A-xi

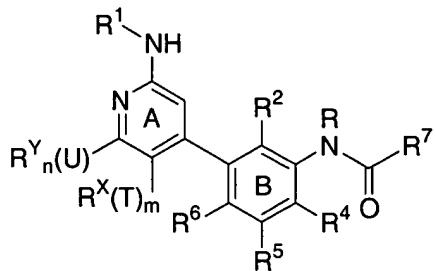


II-A-xii

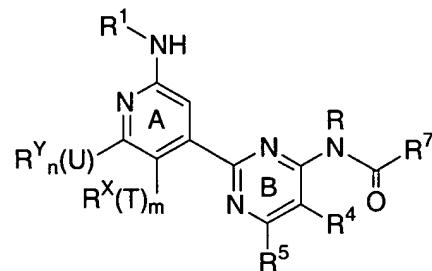


II-A-xiii

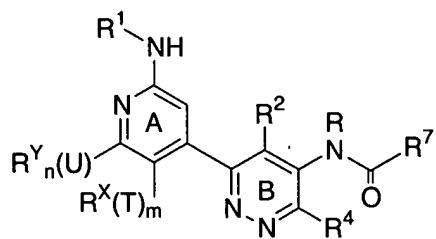
30. The compound of claim 28, wherein for compounds of formula III-A ring B is selected from one of i, ii, iii, iv, v, vii, viii, ix, x, xi, xii, or xiii and compounds have one of formulas III-A-i, III-A-ii, III-A-iii, III-A-iv, III-A-v, III-A-vii, III-A-viii, III-A-ix, III-A-x, III-A-xi, III-A-xii, or III-A-xiii:



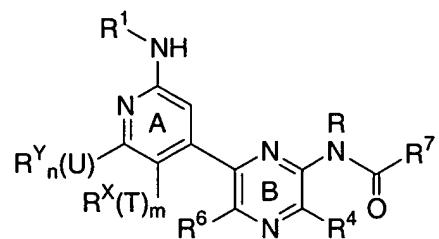
III-A-i



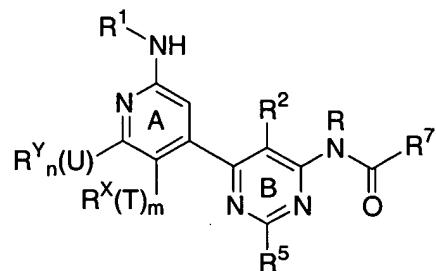
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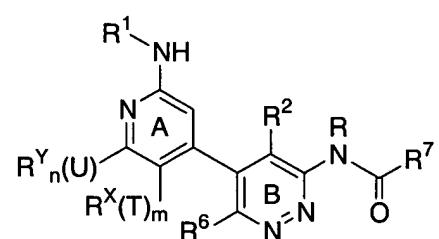
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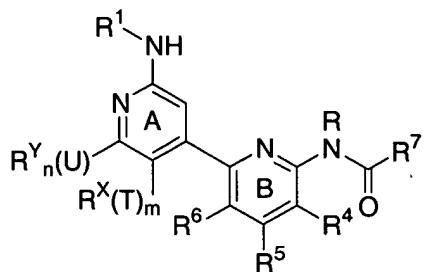
III-A-iv



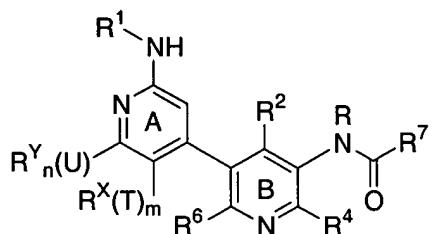
III-A-v



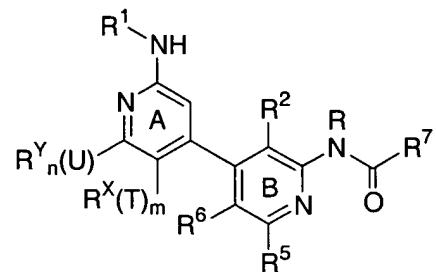
III-A-vii



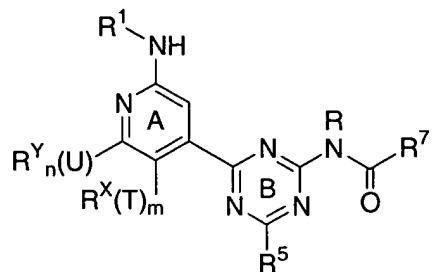
III-A-viii



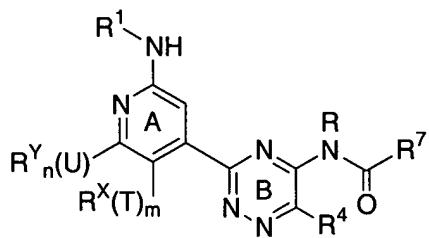
III-A-ix



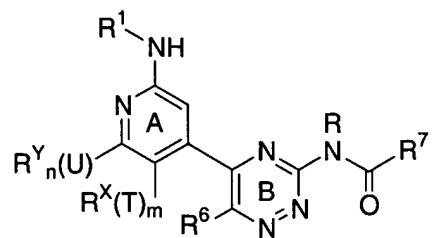
III-A-x



III-A-xi

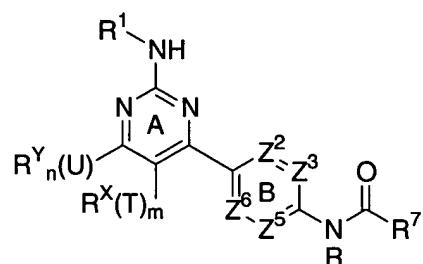


III-A-xii

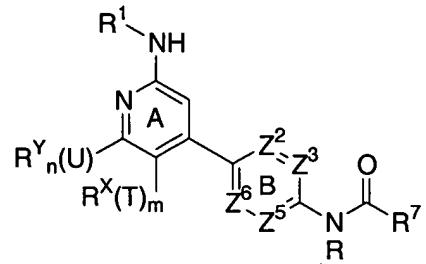


III-A-xiii

31. The compound of claim 1, wherein Z⁴ is CR⁴, and R⁴ is NRC(O)R⁷, wherein R⁷ is (CH₂)_t-Y-R⁸, wherein t is 0, 1 or 2, wherein Y is a bond or is O, S, NR⁹, -OCH₂-, -SCH₂, -NR⁹CH₂, O(CH₂)₂-, -S(CH₂)₂, or -NR⁹(CH₂)₂, and wherein R⁸ is Ar², or R⁸ and R⁹, taken together with the nitrogen atom, form a 5-8 membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen or sulfur, and compounds have one of formulas II-B or III-B:

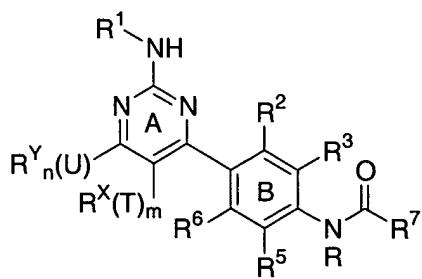


II-B

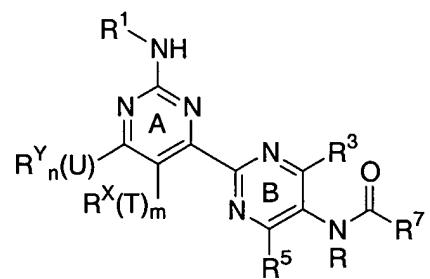


III-B

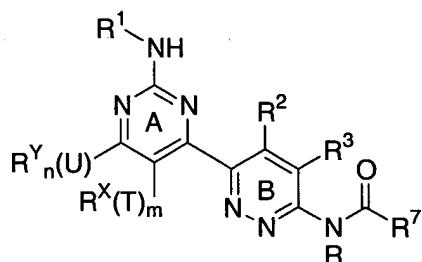
32. The compound of claim 31, wherein for compounds of formula II-B, ring B is selected from i, ii, iii, iv, vi, vii, ix, xii, or xiv and compounds have one of formulas II-B-i, II-B-ii, II-B-iii, II-B-iv, II-B-vi, II-B-vii, II-B-ix, II-B-xii, or II-B-xiv:



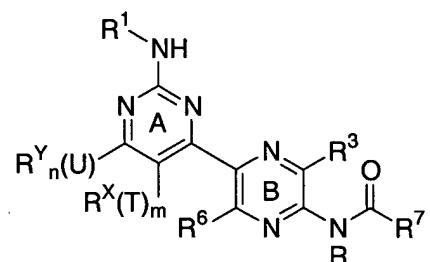
II-B-i



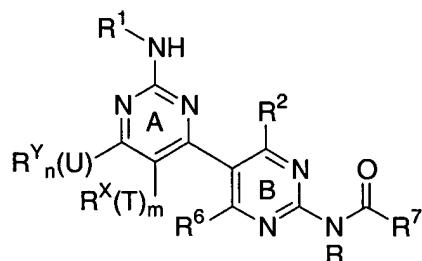
II-B-ii



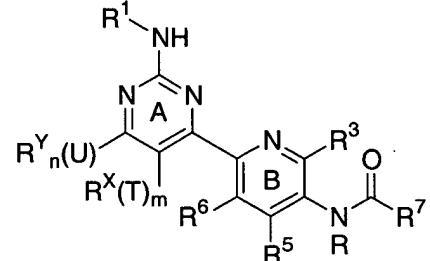
II-B-iii



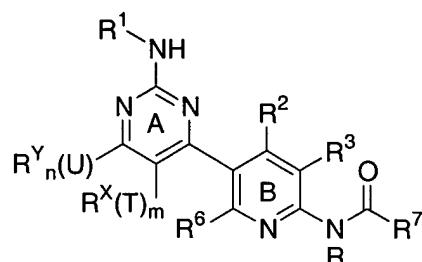
II-B-iv



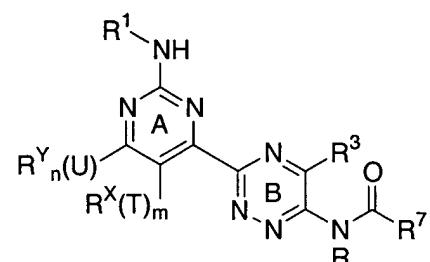
II-B-vi



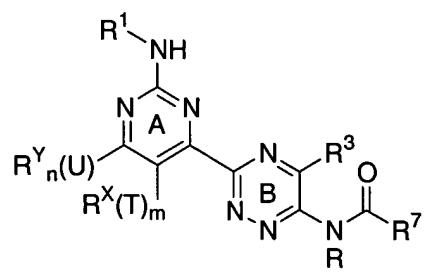
II-B-viii



II-B-ix

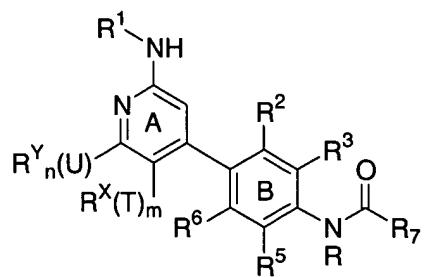


II-B-xii

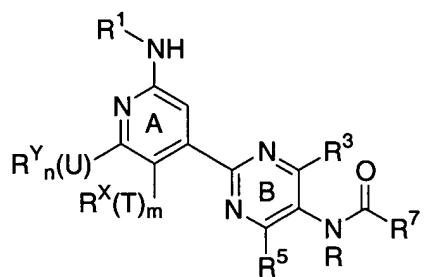


II-B-xiv

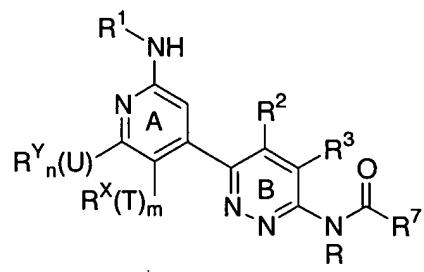
33. The compound of claim 31, wherein for compounds of formula III-B, ring B is selected from i, ii, iii, iv, vi, viii, ix, xii, or xiv and compounds have one of formulas III-B-i, III-B-ii, III-B-iii, III-B-iv, III-B-vi, III-B-viii, III-B-ix, III-B-xii, or III-B-xiv:



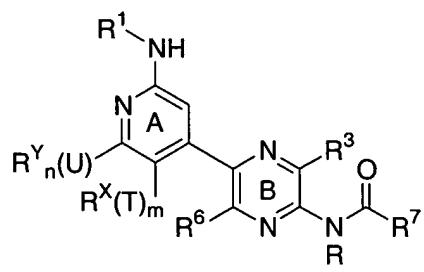
III-B-i



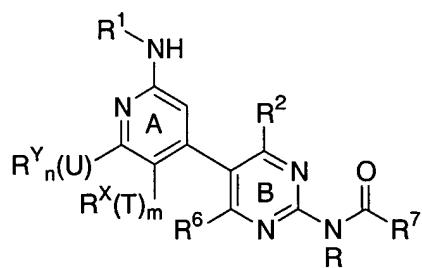
III-B-ii



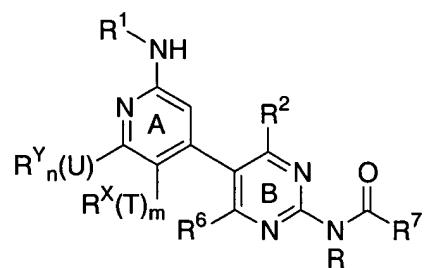
III-B-iii



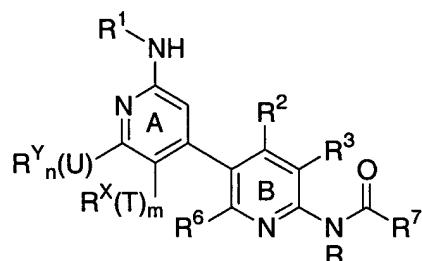
III-B-iv



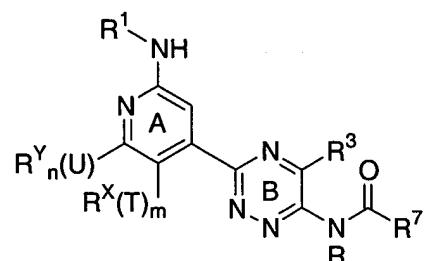
III-B-vi



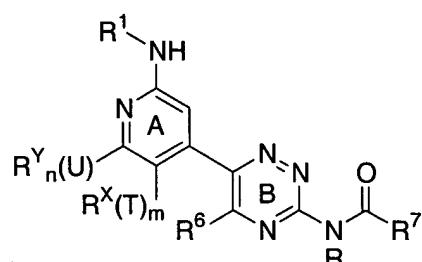
III-B-viii



III-B-ix

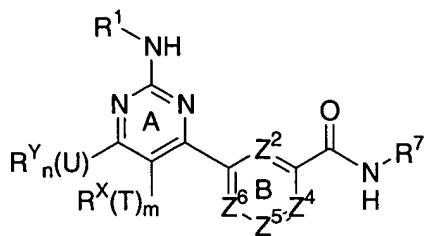


III-B-xii

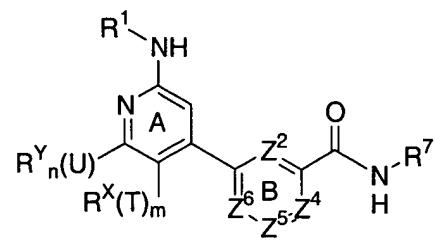


III-B-xiv

34. The compound of claim 1, wherein Z³ or Z⁵ is CR³ or CR⁵, respectively, and R³ or R⁵ is C(O)N(R)(R⁷), wherein R⁷ is (CH₂)_t-Y-R⁸, wherein t is 0, 1 or 2, wherein Y is a bond or is O, S, NR⁹, -OCH₂-, -SCH₂, -NR⁹CH₂, O(CH₂)₂-, -S(CH₂)₂, or -NR⁹(CH₂)₂, and wherein R⁸ is Ar², or R⁸ and R⁹, taken together with the nitrogen atom, form a 5-8 membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen or sulfur and compounds have one of formulas II-C or III-C:

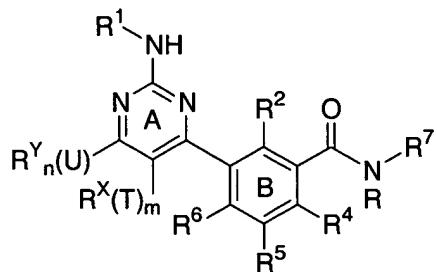


II-C

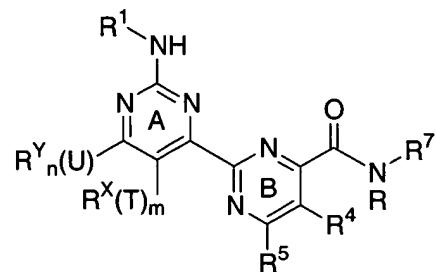


III-C

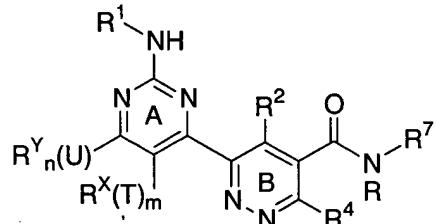
35. The compound of claim 34, wherein for compounds of formula **II-C**, ring B is selected from **i**, **ii**, **iii**, **iv**, **v**, **vii**, **viii**, **ix**, **x**, **xi**, **xii**, or **xiii** and compounds have one of formulas **II-C-i**, **II-C-ii**, **II-C-iii**, **II-C-iv**, **II-C-v**, **II-C-vii**, **II-C-viii**, **II-C-ix**, **II-C-x**, **II-C-xi**, **II-C-xii**, or **II-C-xiii**:



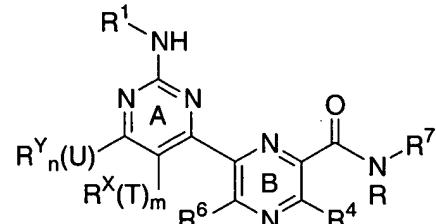
II-C-i



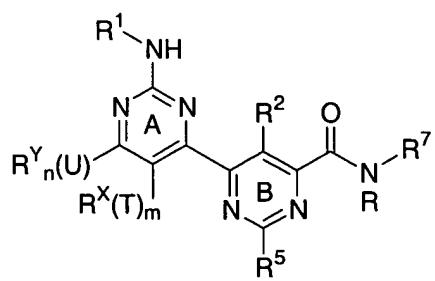
II-C-ii



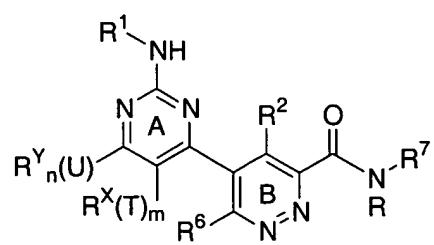
II-C-iii



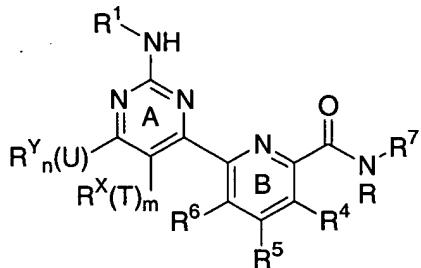
II-C-iv



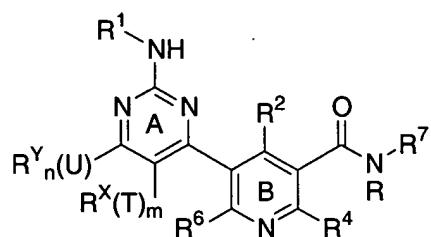
II-C-v



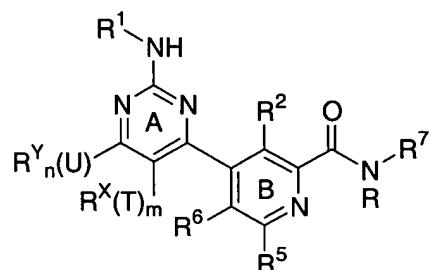
II-C-vii



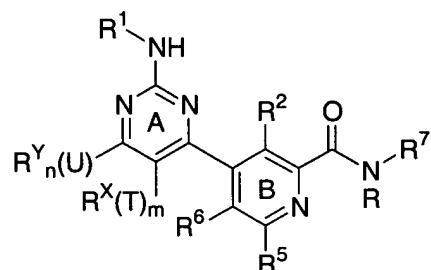
II-C-viii



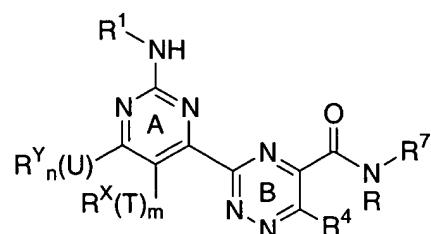
II-C-ix



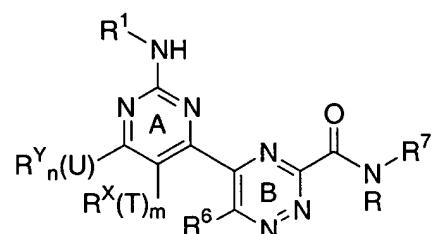
II-C-x



II-C-xi

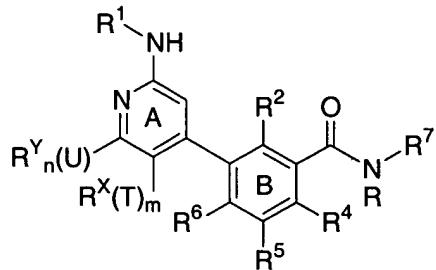


II-C-xii

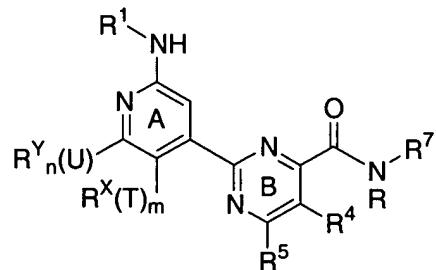


II-C-xiii

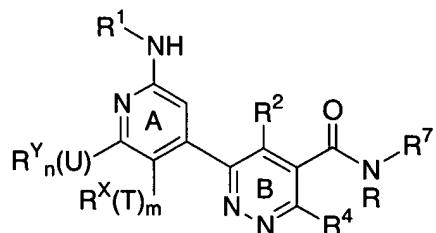
36. The compound of claim 34, wherein for compounds of formula III-C, ring B is selected from i, ii, iii, iv, v, vii, viii, ix, x, xi, xii, or xiii and compounds have one of formulas III-C-i, III-C-ii, III-C-iii, III-C-iv, III-C-v, III-C-vii, III-C-viii, III-C-ix, III-C-x, III-C-xi, III-C-xii, or III-C-xiii are provided as depicted below:



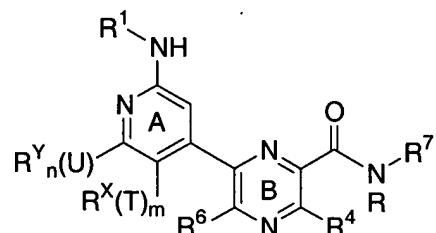
III-C-i



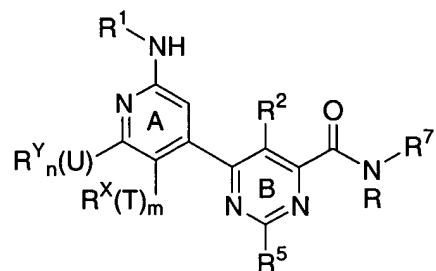
III-C-ii



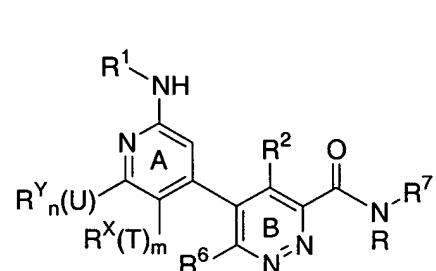
III-C-iii



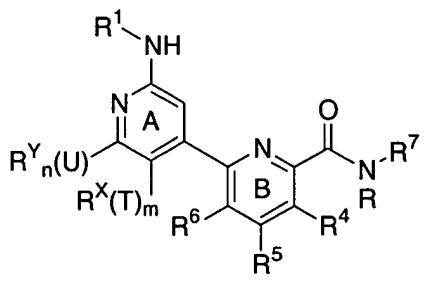
III-C-iv



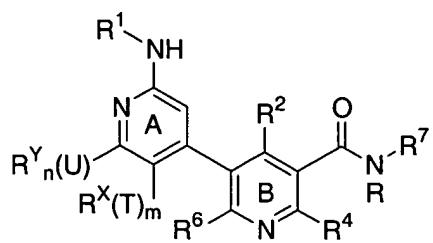
III-C-v



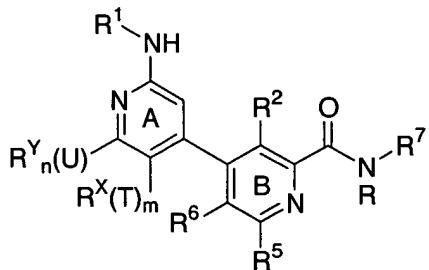
III-C-vii



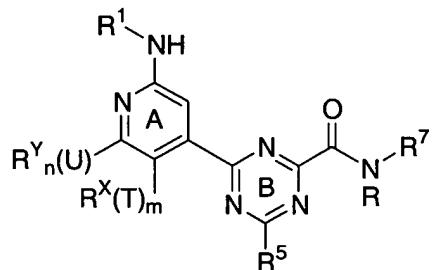
III-C-viii



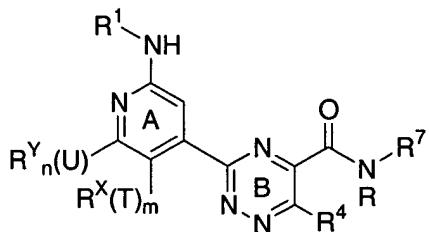
III-C-ix



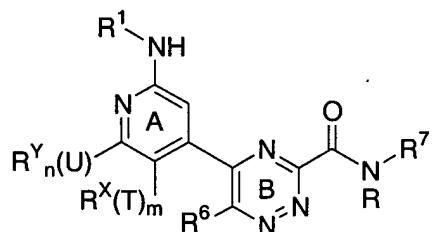
III-C-x



III-C-xi

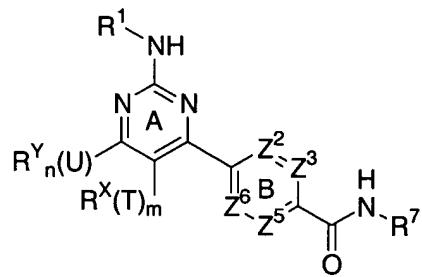


III-C-xii

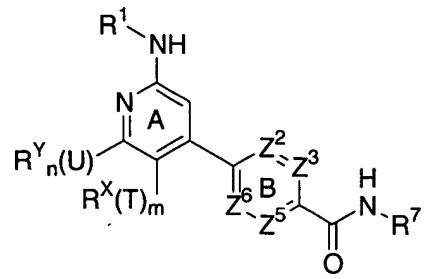


III-C-xiii

37. The compound of claim 1, wherein Z⁴ is CR⁴, and R⁴ is C(O)N(R)(R⁷), wherein R⁷ is (CH₂)_t-Y-R⁸, wherein t is 0, 1 or 2, wherein Y is a bond or is O, S, NR⁹, -OCH₂-, -SCH₂-, NR⁹CH₂, O(CH₂)₂-, -S(CH₂)₂, or -NR⁹(CH₂)₂, and wherein R⁸ is Ar², or R⁸ and R⁹, taken together with the nitrogen atom, form a 5-8 membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen or sulfur and compounds have one of formulas II-D or III-D:

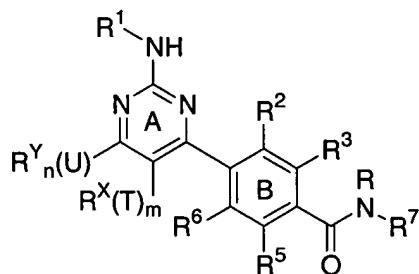


II-D

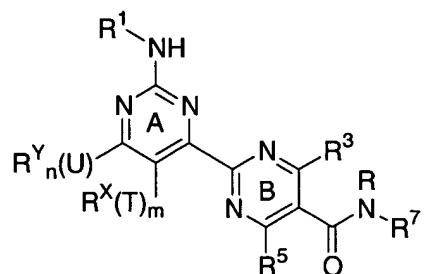


III-D

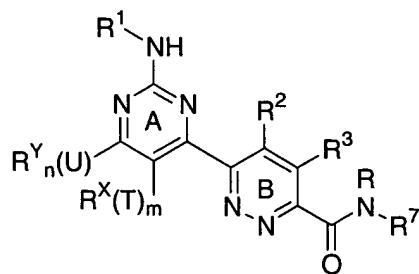
38. The compound of claim 37, wherein for compounds of formula **II-D**, ring B is selected from **i**, **ii**, **iii**, **iv**, **vi**, **vii**, **ix**, **xii**, or **xiv** and compounds have one of formulas **II-D-i**, **II-D-ii**, **II-D-iii**, **II-D-iv**, **II-D-vi**, **II-D-vii**, **II-D-ix**, **II-D-xii**, or **II-D-xiv**:



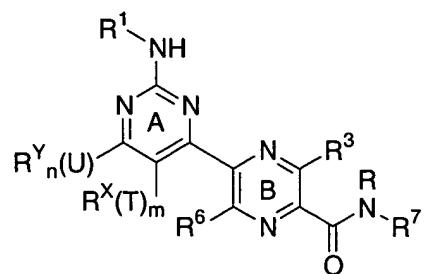
II-D-i



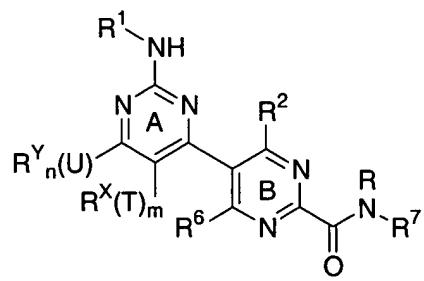
II-D-ii



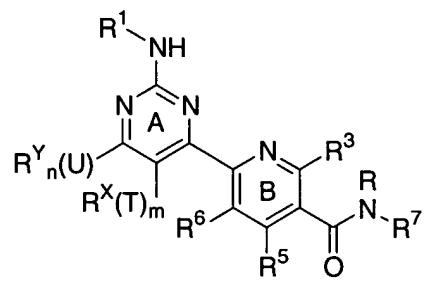
II-D-iii



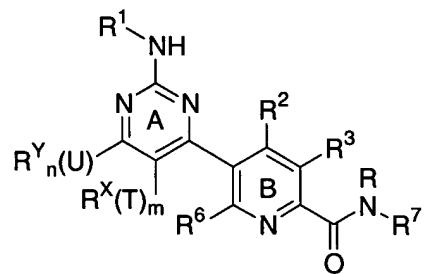
II-D-iv



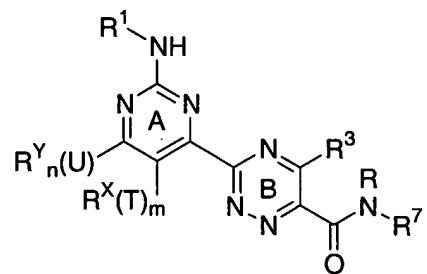
II-D-vi



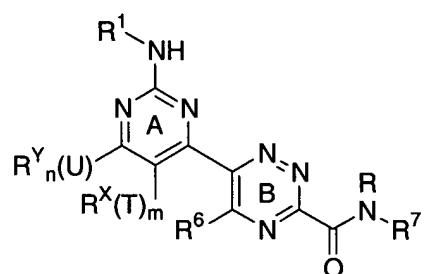
II-D-viii



II-D-ix

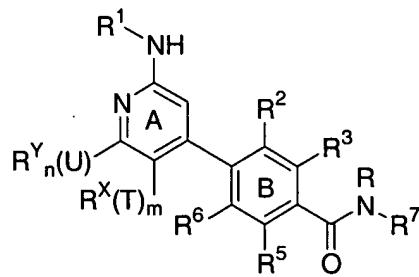


II-D-xii

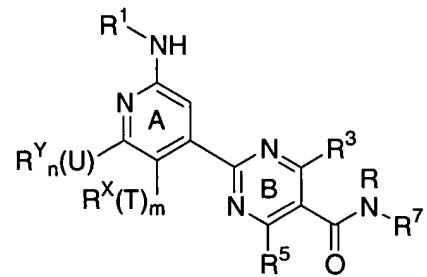


II-D-xiv

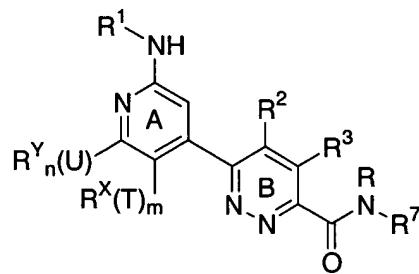
39. The compound of claim 37, wherein for compounds of formula III-D, ring B is selected from i, ii, iii, iv, vi, viii, ix, xii, or xiv and compounds have one of formulas III-D-i, III-D-ii, III-D-iii, III-D-iv, III-D-vi, III-D-viii, III-D-ix, III-D-xii, or III-D-xiv:



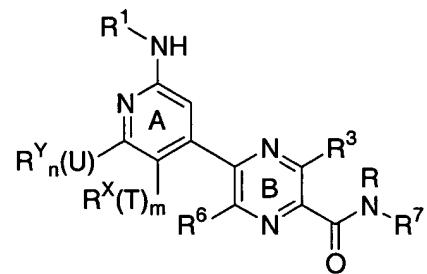
III-D-i



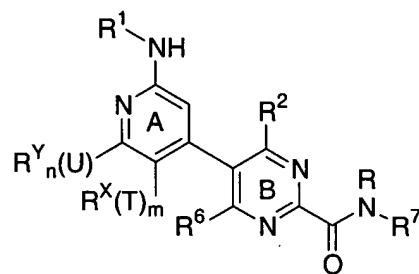
III-D-ii



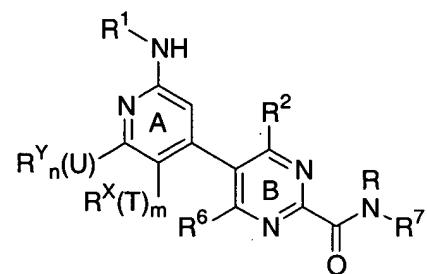
III-D-iii



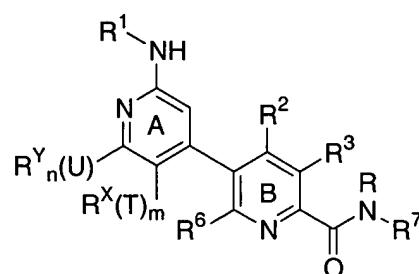
III-D-iv



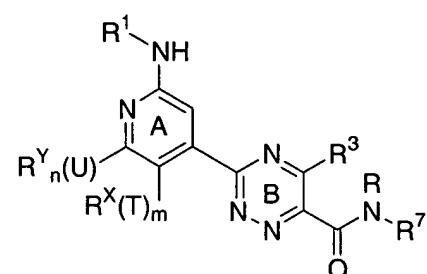
III-D-vi



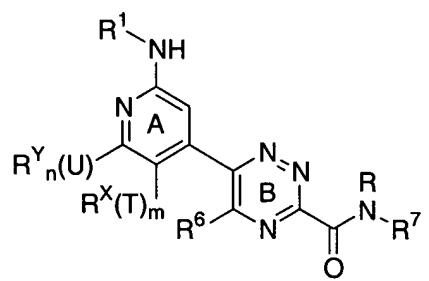
III-D-viii



III-D-ix

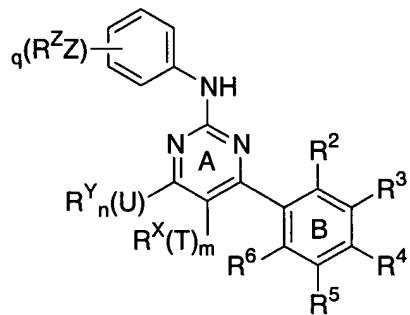


III-D-xii

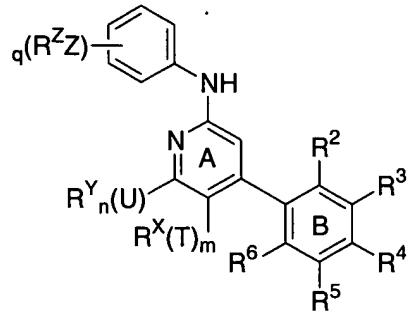


III-D-xiv

40. The compound of claim 1, where R^1 is optionally substituted phenyl and ring B is an optionally substituted phenyl group and compounds have the general formulas **IV** or **V**:

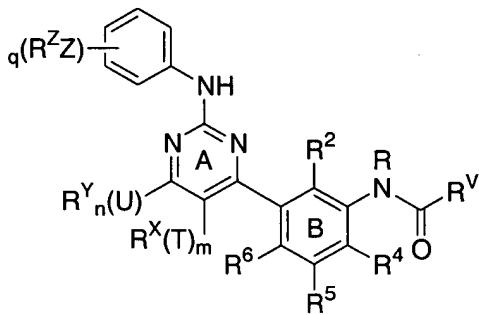


IV

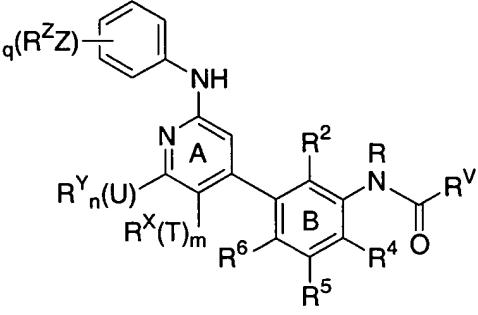


V

41. The compound of claim 40, wherein, R^3 is $NRCOR^7$ and compounds have the general formulae **IV-A-(i)** or **V-A-(i)**:

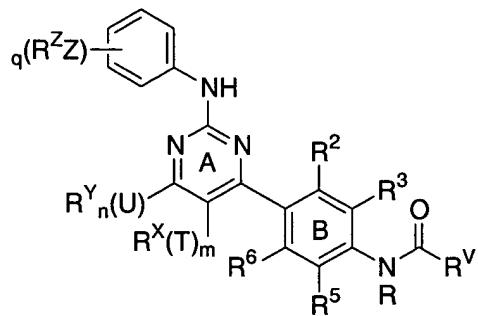


IV-A-(i)

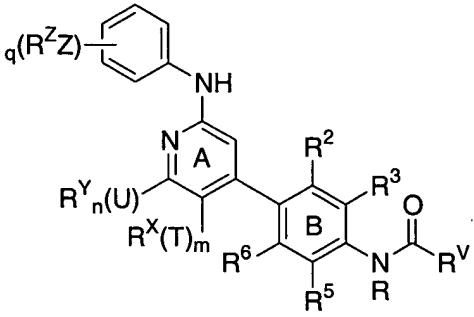


V-A-(i)

42. The compound of claim 40, wherein R^4 is $NRCOR^7$ and compounds have the general formulae **IV-B-(i)** or **V-B-(i)**:

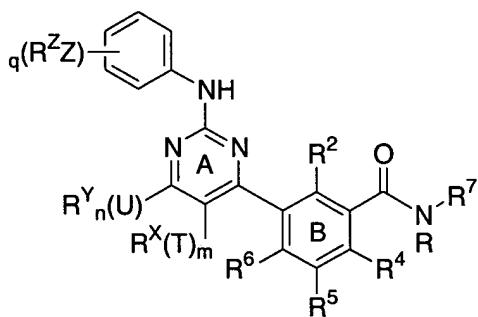


IV-B-(i)

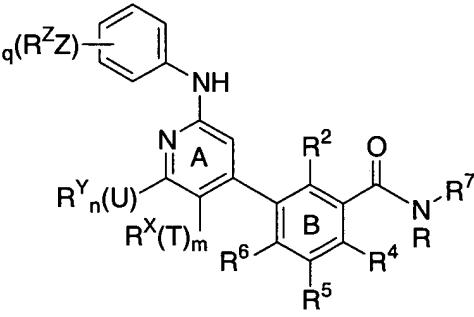


V-B-(i)

43. The compound of claim 40, wherein R^3 is $CONRR^7$ and compounds have the general formulae **IV-C-(i)** or **V-C-(i)**:

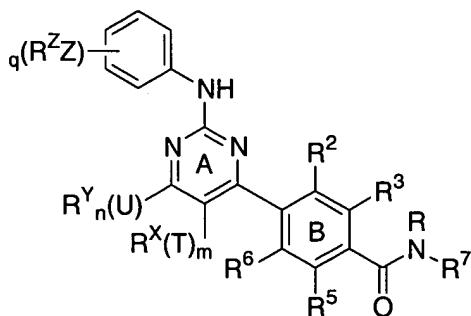


IV-C-(i)

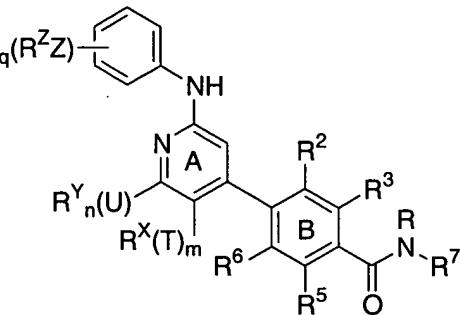


V-C-(i)

44. The compound of claim 40, wherein R^4 is $CONRR^7$ and compounds have the general formulae **IV-D-(i)** or **VII-D-(i)**:

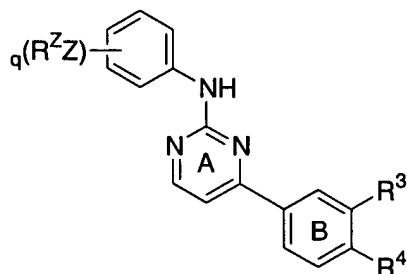


IV-D-(i)

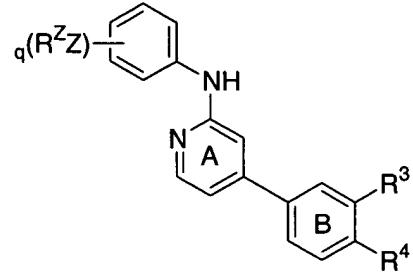


V-D-(i)

45. The compound of claim 40, wherein R¹ is optionally substituted phenyl, ring A is pyrimidinyl or pyridyl, ring B is phenyl, and R², R⁵, and R⁶ are each hydrogen, and compounds have the general formulae VI and VII:



VI



VII

46. The compound of claim 40 or 45, wherein

- a. q is 0 or 1 and ZR^Z is -NH₂, -OH, C₁₋₄alkoxy, or -SO₂NH₂;
- b. R³ is NRCOR⁷, wherein R⁷ is (CH₂)_t-Y-R⁸, and t is 0, Y is a bond, and R⁸ is phenyl (**a**), or is an optionally substituted heteroaryl moiety selected from one of groups **b** through **r**, and wherein r is 0 or 1, and WR^W substituents are halogen, C₁₋₄alkyl, -(R)₂, -OR, -SR, -SO₂N(R)₂, -N(R)SO₂R, -N(R)COR, -N(R)₂, -CH₂OR, -CH₂N(R)₂, or -CH₂SR; and
- c. R⁴ is hydrogen.

47. The compound of claim 40 or 45, wherein:

- a. q is 0 or 1 and ZR^Z is -NH₂, -OH, C₁₋₄alkoxy, or -SO₂NH₂;

- b. R^3 is $CONRR^7$, wherein R^7 is $(CH_2)_t-Y-R^8$, and t is 0, Y is a bond, and R^8 is phenyl (**a**) or is an optionally substituted heteroaryl moiety selected from one of groups **b** through **r**, and wherein r is 0 or 1, and WR^W substituents are halogen, C₁₋₄alkyl, -(R)₂, -OR, -SR, -SO₂N(R)₂, -N(R)SO₂R, -N(R)COR, -N(R)₂, -CH₂OR, -CH₂N(R)₂, or -CH₂SR; and
- c. R^4 is hydrogen.

48. The compound of claim 40 or 45, wherein:

- a. q is 0 or 1 and ZR^Z is -NH₂, -OH, C₁₋₄alkoxy, or -S(O)₂NH₂;
- b. R^4 is $NRCOR^7$, wherein R^7 is $(CH_2)_t-Y-R^8$, and t is 0, Y is a bond, and R^8 is phenyl (**a**) or an optionally substituted heteroaryl moiety selected from one of groups **b** through **z**, and wherein r is 0 or 1, and WR^W substituents are halogen, C₁₋₄alkyl, -(R)₂, -OR, -SR, -SO₂N(R)₂, -N(R)SO₂R, -N(R)COR, -N(R)₂, -CH₂OR, -CH₂N(R)₂, or -CH₂SR; and
- c. R^3 is hydrogen.

49. The compound of claim 40 or 45, wherein:

- a. q is 0 or 1 and ZR^Z is -NH₂, -OH, C₁₋₄alkoxy, or -S(O)₂NH₂;
- b. R^4 is $CONRR^7$, wherein R^7 is $(CH_2)_t-Y-R^8$, and t is 0, Y is a bond, and R^8 is phenyl (**a**) or an optionally substituted heteroaryl moiety selected from one of groups **b** through **z**, and wherein r is 0 or 1, and WR^W substituents are halogen, C₁₋₄alkyl, -(R)₂, -OR, -SR, -SO₂N(R)₂, -N(R)SO₂R, -N(R)COR, -N(R)₂, -CH₂OR, -CH₂N(R)₂, or -CH₂SR; and
- c. R^3 is hydrogen.

50. The compound of claim 40 or 45, wherein:

- a. q is 0 or 1 and ZR^Z is -NH₂, -OH, C₁₋₄alkoxy, or -S(O)₂NH₂;
- b. R^3 is $NRCOR^7$, wherein R^7 is $(CH_2)_t-Y-R^8$, and t is 0 or 1, Y is NR⁹, and R⁸ and R⁹, taken together with the nitrogen atom, form a group selected from **s**, **t**, **u**, or **v**, and wherein r is 0 or 1, and WR^W substituents are halogen, C₁₋₄alkyl, -(R)₂, -OR, -SR, -SO₂N(R)₂, -N(R)SO₂R, -N(R)COR, -N(R)₂, -CH₂OR, -CH₂N(R)₂, or -CH₂SR; and

c. R^4 is hydrogen.

51. The compound of claim 40 or 45, wherein:

- a. q is 0 or 1 and ZR^Z is $-NH_2$, $-OH$, $C_{1-4}alkoxy$, or $-S(O)_2NH_2$;
- b. R^3 is $CONRR^7$, wherein R^7 is $(CH_2)_t-Y-R^8$, and t is 0 or 1, Y is NR^9 , and R^8 and R^9 , taken together with the nitrogen atom, form a group selected from **s**, **t**, **u**, or **v**, and wherein r is 0 or 1, and WR^W substituents are halogen, $C_{1-4}alkyl$, $-(R)_2$, $-OR$, $-SR$, $-SO_2N(R)_2$, $-N(R)SO_2R$, $-N(R)COR$, $-N(R)_2$, $-CH_2OR$, $-CH_2N(R)_2$, or $-CH_2SR$; and
- c. R^4 is hydrogen.

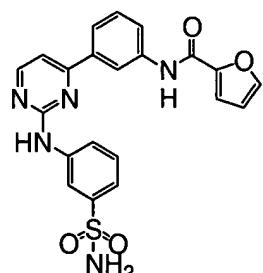
52. The compound of claim 40 or 45, wherein:

- a. q is 0 or 1 and ZR^Z is $-NH_2$, $-OH$, $C_{1-4}alkoxy$, or $-S(O)_2NH_2$;
- b. R^4 is $NRCOR^7$, wherein R^7 is $(CH_2)_t-Y-R^8$, and t is 0 or 1, Y is NR^9 , and R^8 and R^9 , taken together with the nitrogen atom, form a group selected from **s**, **t**, **u**, or **v**, and wherein r is 0 or 1, and WR^W substituents include halogen, $C_{1-4}alkyl$, NH_2 , OH , SH , SO_2NH_2 , $C_{1-4}alkoxy$, $C_{1-4}thioalkyl$, CH_2OR , $CH_2N(R)_2$, or CH_2SR ; and
- c. R^3 is hydrogen.

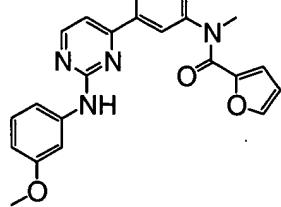
53. The compound of claim 40 or 45, wherein:

- a. q is 0 or 1 and ZR^Z is $-NH_2$, $-OH$, $C_{1-4}alkoxy$, or $-S(O)_2NH_2$;
- b. R^4 is $CONRR^7$, wherein R^7 is $(CH_2)_t-Y-R^8$, and t is 0 or 1, Y is NR^9 , and R^8 and R^9 , taken together with the nitrogen atom, form a group selected from **s**, **t**, **u**, or **v**, and wherein r is 0 or 1, and WR^W substituents are halogen, $C_{1-4}alkyl$, $-(R)_2$, $-OR$, $-SR$, $-SO_2N(R)_2$, $-N(R)SO_2R$, $-N(R)COR$, $-N(R)_2$, $-CH_2OR$, $-CH_2N(R)_2$, or $-CH_2SR$; and
- c. R^3 is hydrogen.

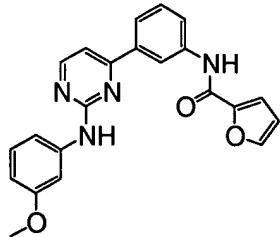
54. The compound of claim 1, having one of the following structures:



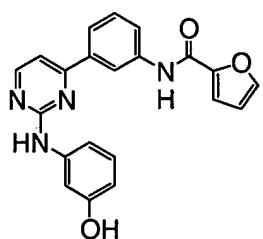
IV-A(i)-1



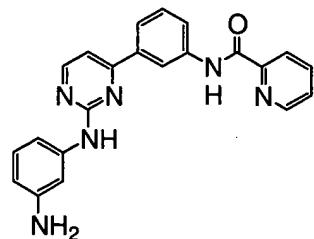
IV-A(i)-2



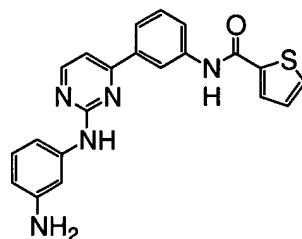
IV-A(i)-3



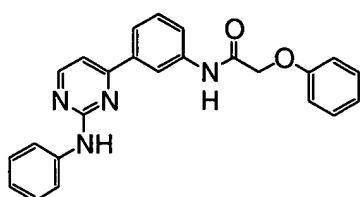
IV-A(i)-4



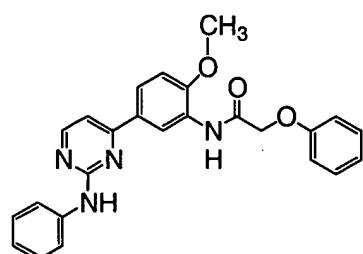
IV-A(i)-5



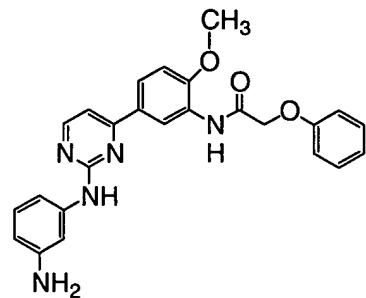
IV-A(i)-6



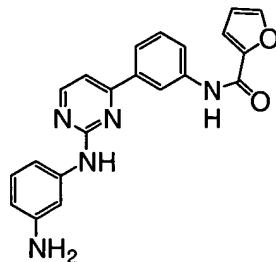
IV-A(i)-7



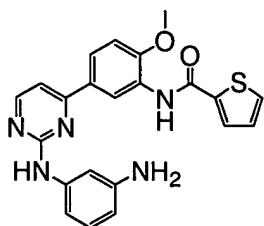
IV-A(i)-8



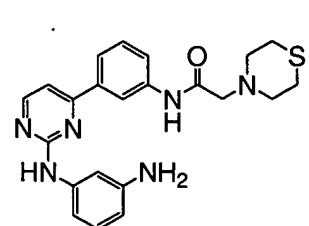
IV-A(i)-9



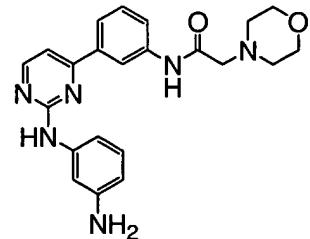
IV-A(i)-10



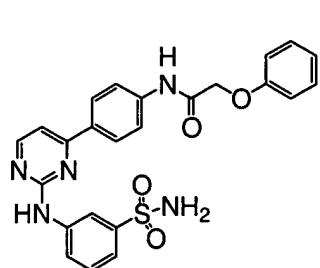
IV-A(i)-11



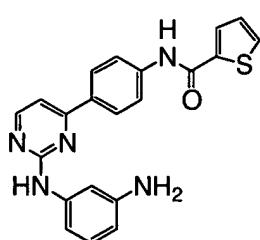
IV-A(i)-12



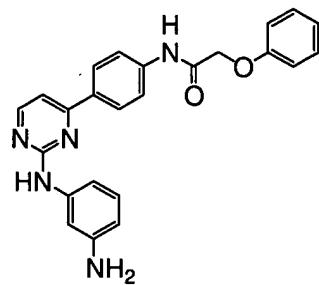
IV-A(i)-13



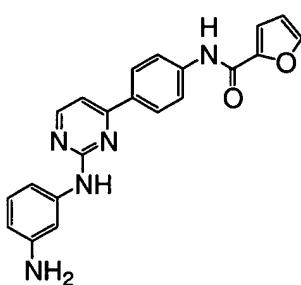
IV-B(i)-1



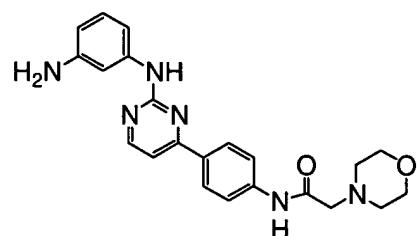
IV-B(i)-2



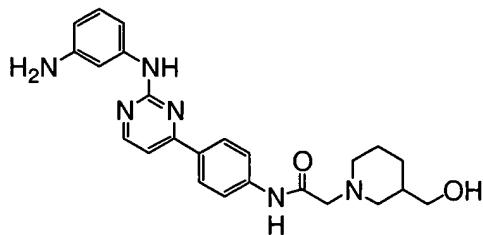
IV-B(i)-3



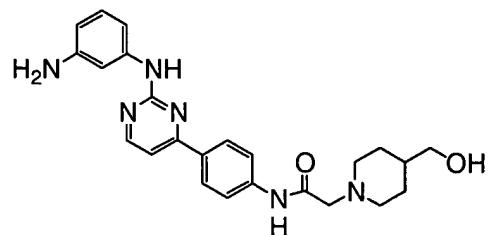
IV-B(i)-4



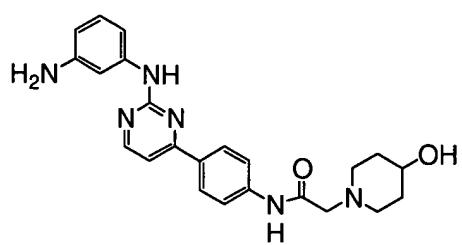
IV-B(i)-5



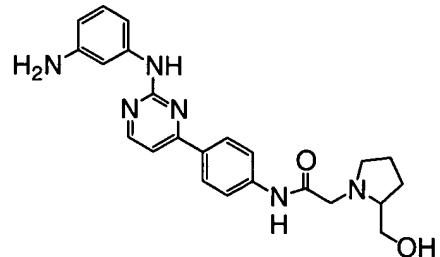
IV-B(i)-6



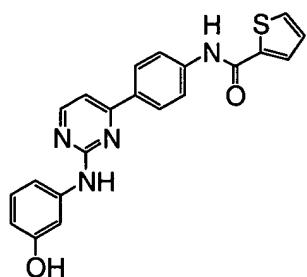
IV-B(i)-7



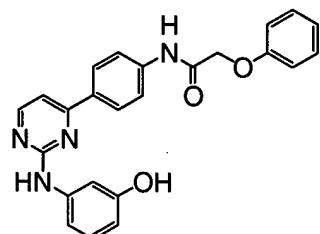
IV-B(i)-8



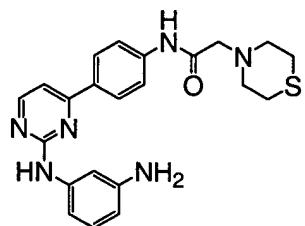
IV-B(i)-9



IV-B(i)-10



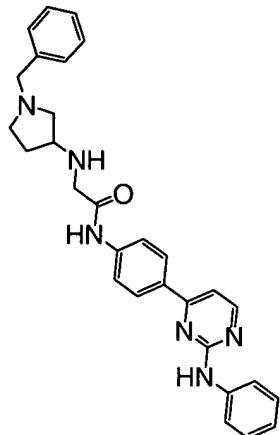
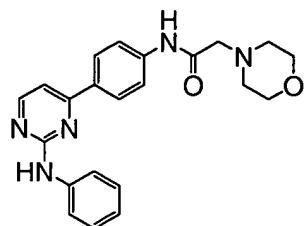
IV-B(i)-11



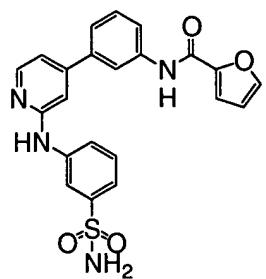
IV-B(i)-12



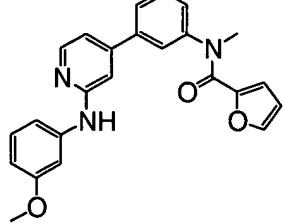
IV-B(i)-13



IV-B(i)-14

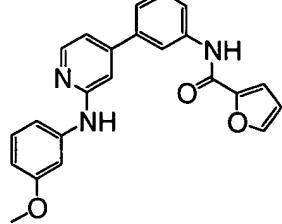


V-A(i)-1

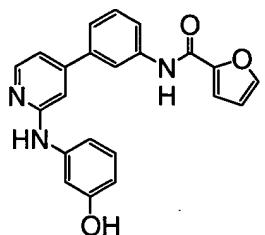


V-A(i)-2

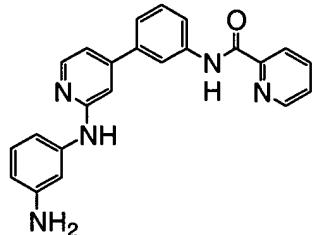
IV-B(i)-15



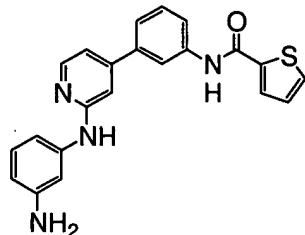
V-A(i)-3



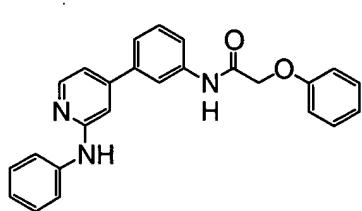
V-A(i)-4



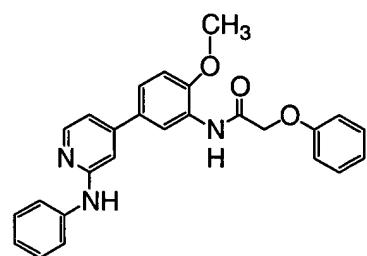
V-A(i)-5



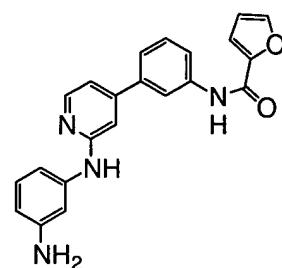
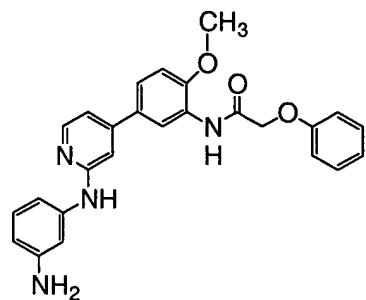
V-A(i)-6



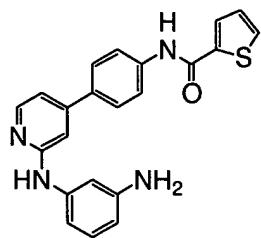
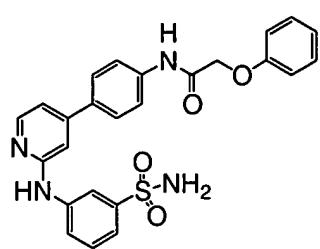
V-A(i)-7



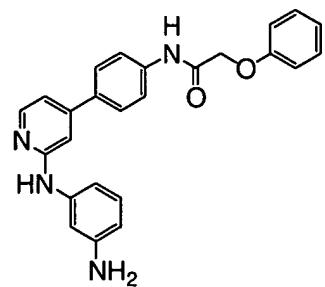
V-A(i)-8



V-A(i)-9



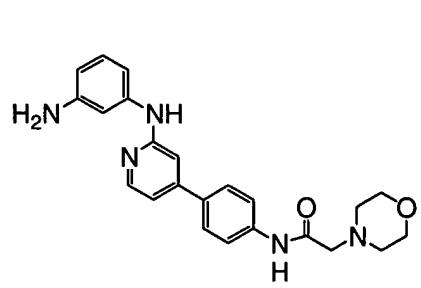
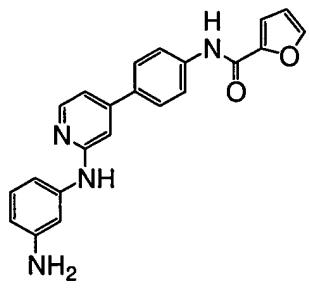
V-A(i)-10



V-B(i)-1

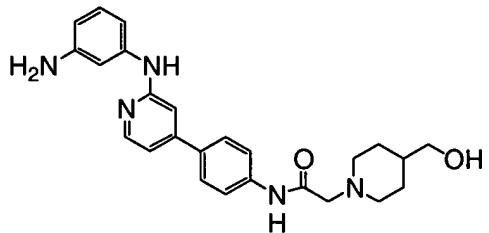
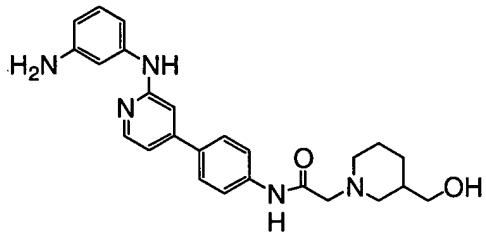
V-B(i)-2

V-B(i)-3



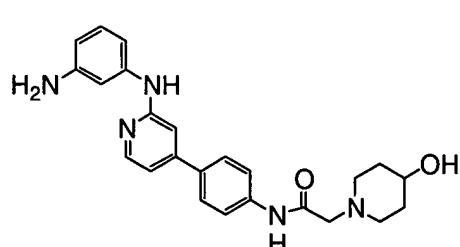
V-B(i)-4

V-B(i)-5

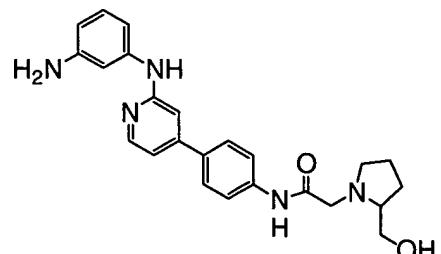


V-B(i)-6

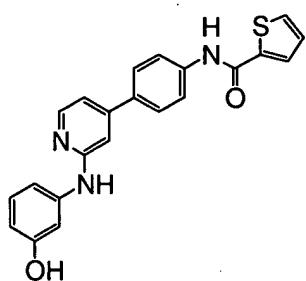
V-B(i)-7



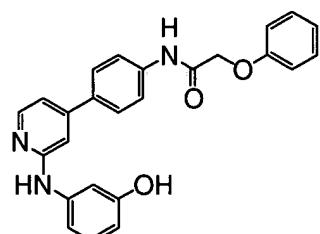
V-B(i)-8



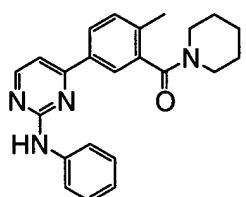
V-B(i)-9



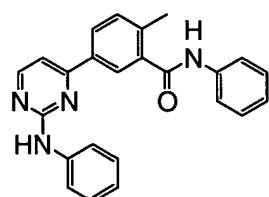
V-B(i)-10



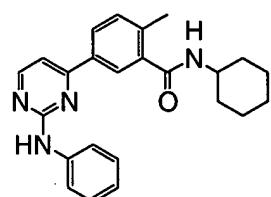
V-B(i)-11



IV-C(i)-1



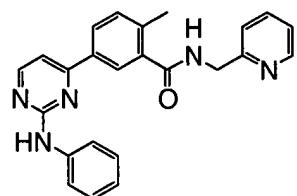
IV-C(i)-2



IV-C(i)-3



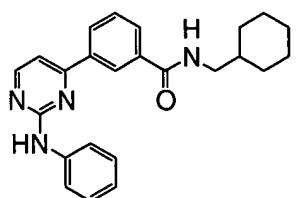
IV-C(i)-4



IV-C(i)-5



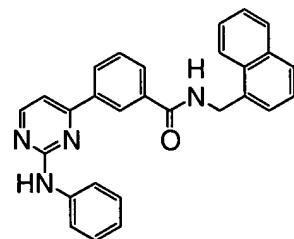
IV-C(i)-6



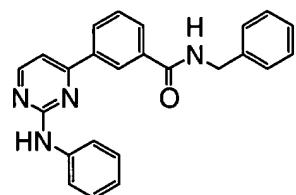
IV-C(i)-7



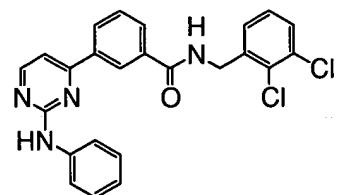
IV-C(i)-8



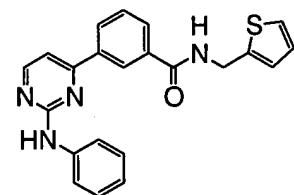
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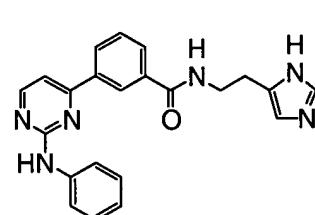
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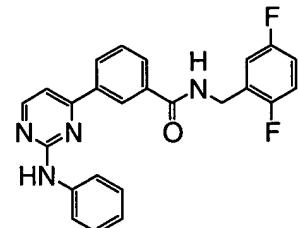
IV-C(i)-11



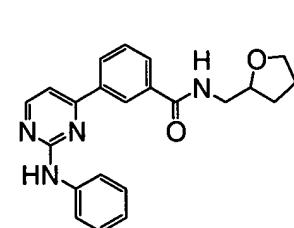
IV-C(i)-12



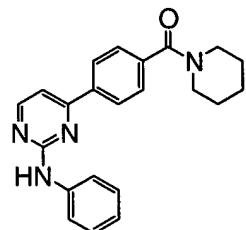
IV-C(i)-13



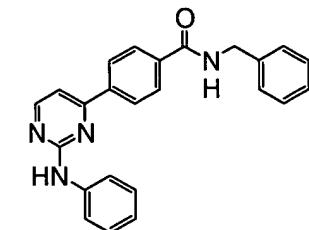
IV-C(i)-14



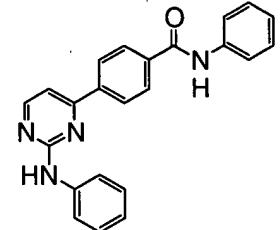
IV-C(i)-15



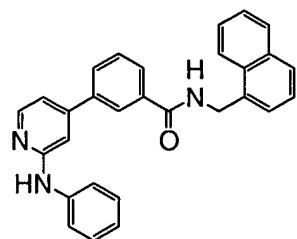
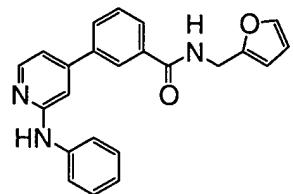
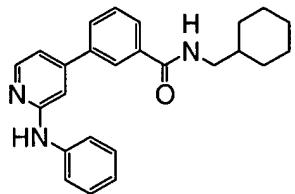
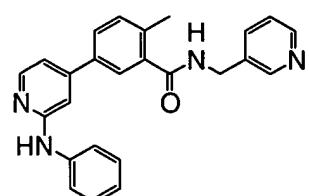
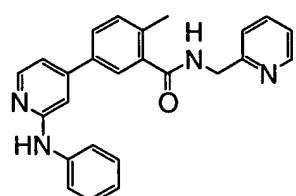
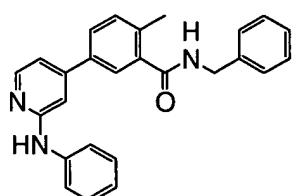
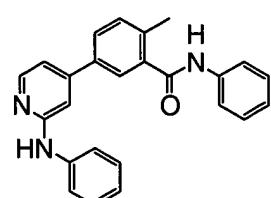
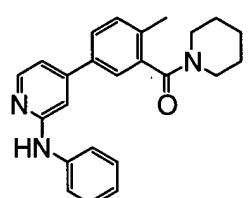
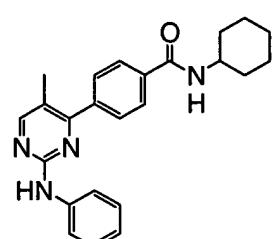
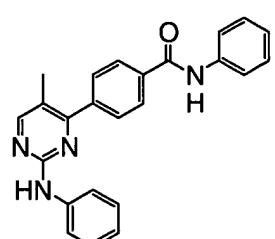
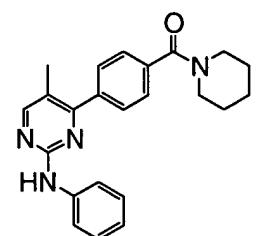
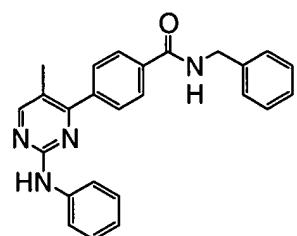
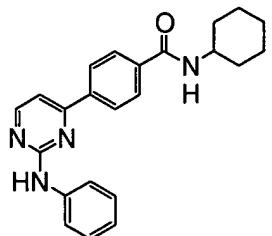
IV-D(i)-1



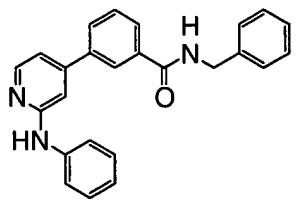
IV-D(i)-2



IV-D(i)-3



V-C(i)-7



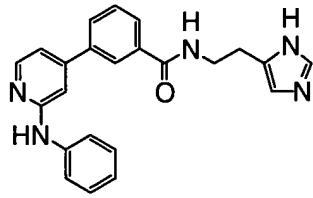
V-C(i)-8



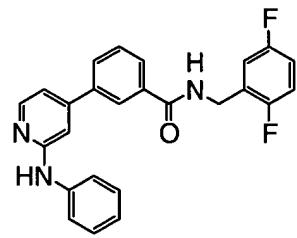
V-C(i)-9



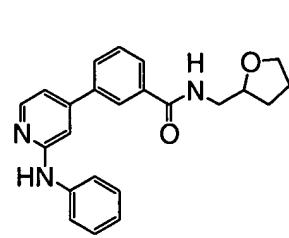
V-C(i)-10



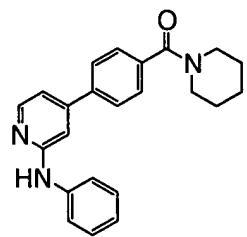
V-C(i)-11



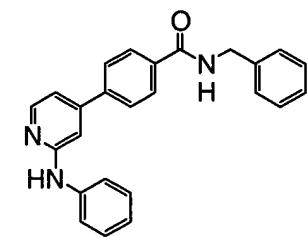
V-C(i)-12



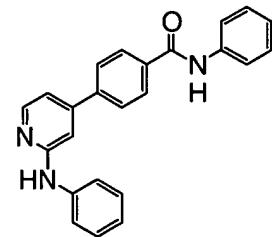
V-C(i)-13



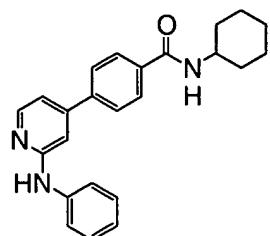
V-C(i)-14



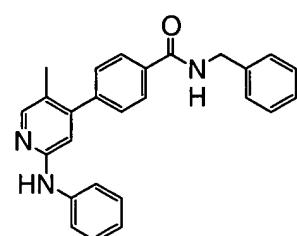
V-C(i)-15



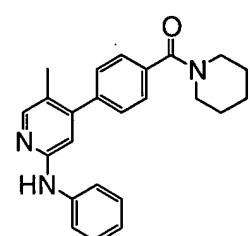
V-D(i)-1



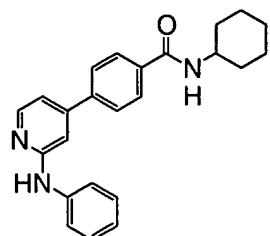
V-D(i)-2



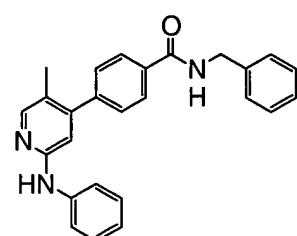
V-D(i)-3



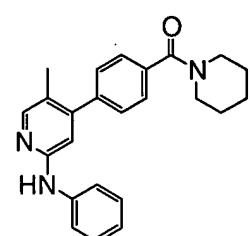
V-D(i)-4

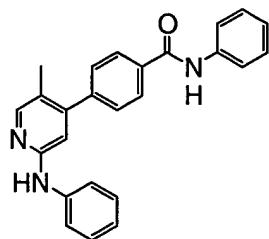


V-D(i)-5

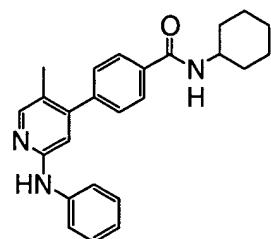


V-D(i)-6





V-D(i)-7



V-D(i)-8

55. A pharmaceutical composition comprising a compound according to claim 1, and a pharmaceutically acceptable carrier, adjuvant, or vehicle.

56. The composition of claim 55, further comprising an additional therapeutic agent selected from a chemotherapeutic or anti-proliferative agent, a treatment for Alzheimer's Disease, a treatment for Parkinson's Disease, an agent for treating Multiple Sclerosis (MS), a treatment for asthma, an agent for treating schizophrenia, an anti-inflammatory agent, an immunomodulatory or immunosuppressive agent, a neurotrophic factor, an agent for treating cardiovascular disease, an agent for treating destructive bone disorders, an agent for treating liver disease, an agent for treating a blood disorder, or an agent for treating an immunodeficiency disorder.

57. A method of inhibiting JAK kinase activity in a biological sample or a patient, comprising the step of contacting said biological sample or patient with:

- a) the composition of claim 55; or
- b) the compound of claim 1.

58. A method of treating or lessening the severity of a disease or disorder selected from an immune response, an autoimmune disease, a neurodegenerative disorder, or a solid or hematologic malignancy comprising administering to a patient in need thereof a compound of claim 1 or a composition of claim 55.

59. The method of claim 58, wherein the disease is an allergic or type I hypersensitivity reaction, asthma, transplant rejection, graft versus host disease, rheumatoid arthritis, amyotrophic lateral sclerosis, multiple sclerosis, Familial amyotrophic lateral sclerosis (FALS), leukemia, or lymphoma.